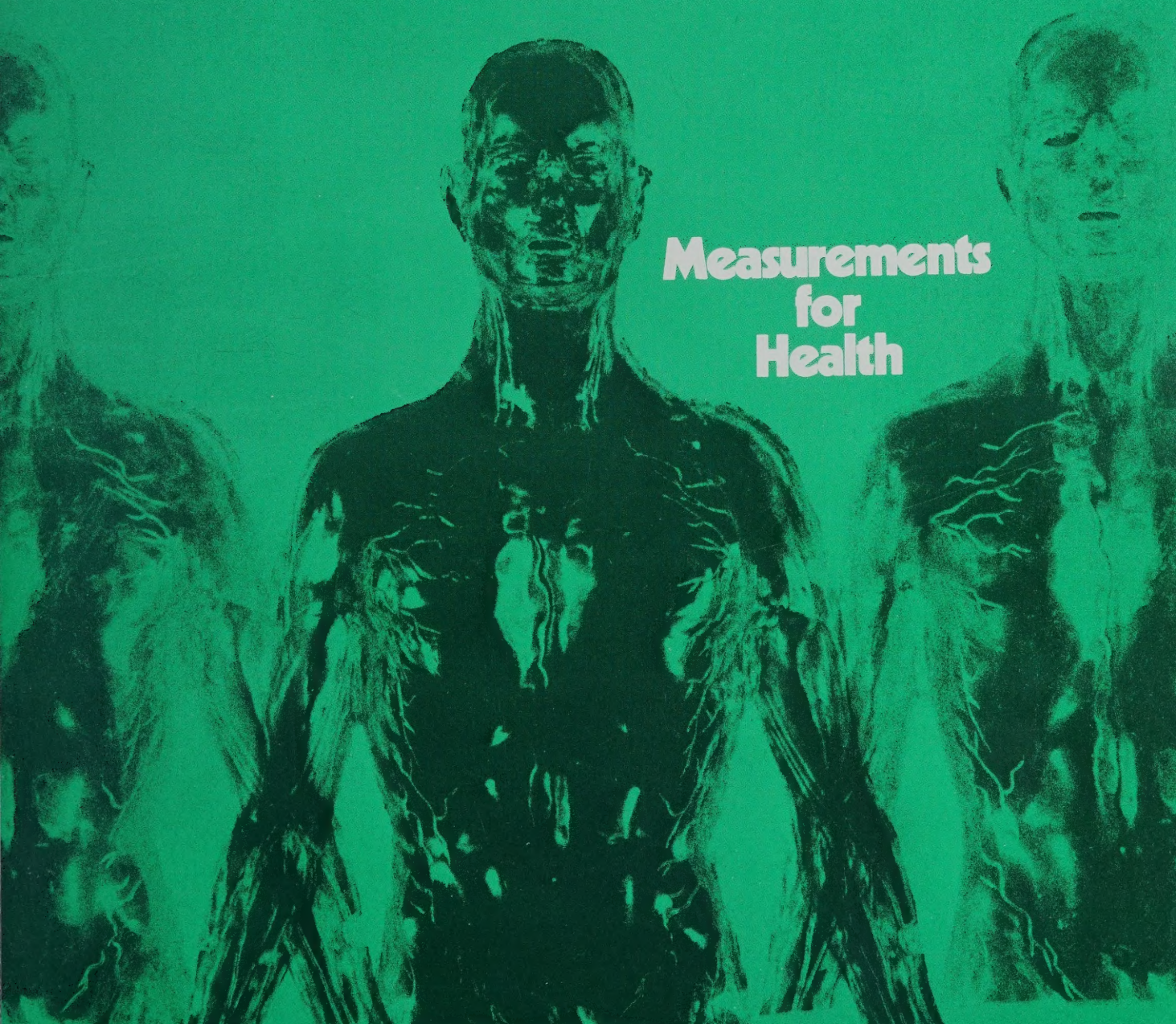


THE TECHNICAL NEWS BULLETIN OF THE NATIONAL BUREAU OF STANDARDS May 1974

DIMENSIONS

NBS



**Measurements
for
Health**

A PUBLICATION OF THE UNITED STATES DEPARTMENT OF COMMERCE

DIMENSIONS

NBS

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Today, because improved medical diagnosis and therapy require accurate measurement and standardization, the Bureau's expertise in the physical, engineering and information sciences is providing a needed link with the medical community to solve urgent problems.

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The National Bureau of Standards serves as a focal point in the Federal Government for assuring maximum application of the physical and engineering sciences to the advancement of technology in industry and commerce. For this purpose, the Bureau is organized as follows:

The Institute for Basic Standards
The Institute for Materials Research
The Institute for Applied Technology
The Institute for Computer Sciences and Technology

Center for Radiation Research
Center for Building Technology
Center for Consumer Product Safety

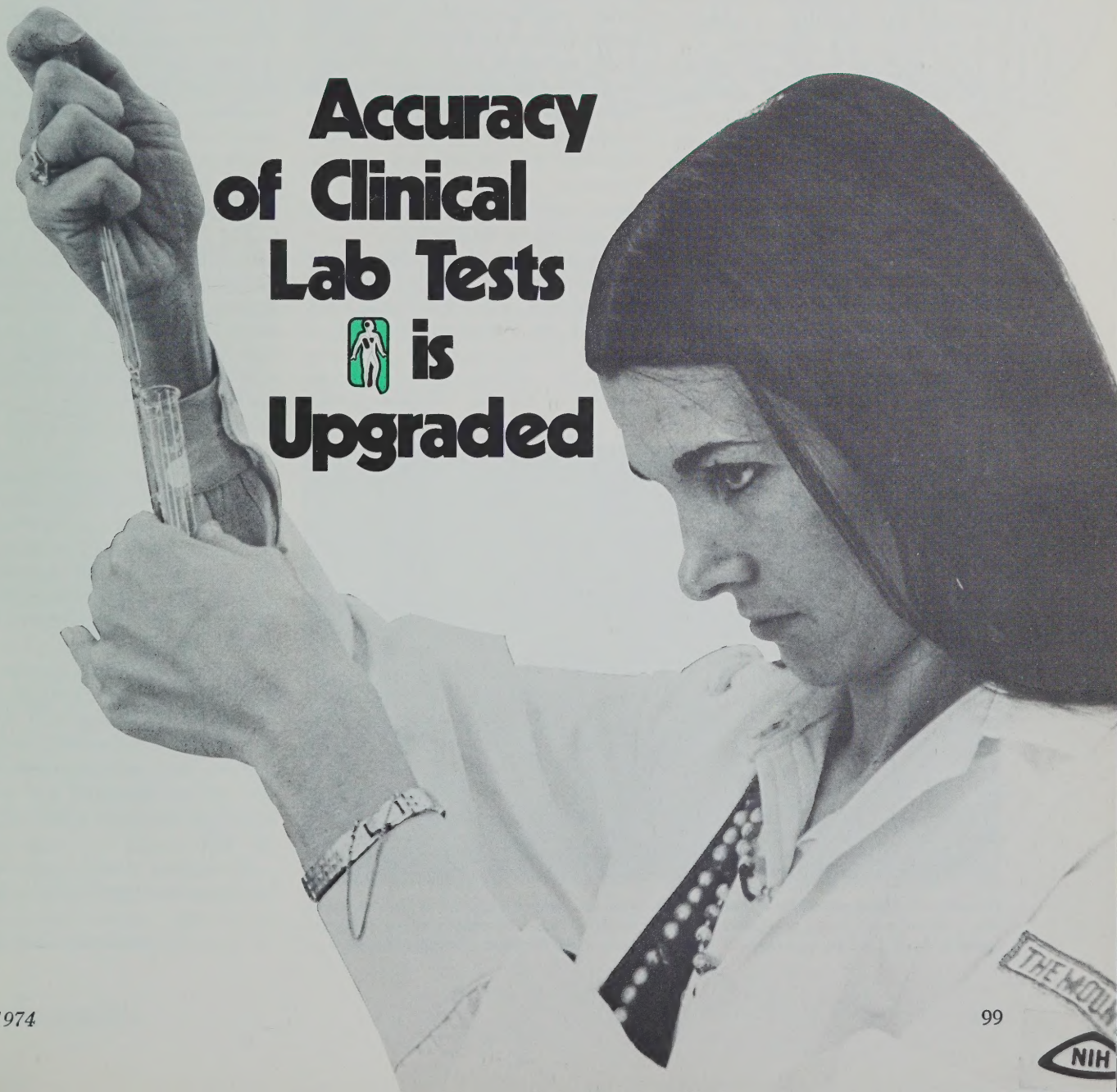
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DR. DAVID J. SPENCER, Director of the Department of Health, Education, and Welfare's (HEW) Center for Disease Control in Atlanta, set members of the medical profession back on their heels in 1967 when he stated that 25 percent of all clinical laboratory tests were so poorly performed as to be medically useless.

turn page

Accuracy of Clinical Lab Tests is Upgraded



CLINICAL LABS *continued*

Testimony by Dr. David Spencer, a respected HEW official, before Congress made a significant impact and helped produce the Clinical Laboratory Improvement Act of 1967.

That the Act was needed can be attested to by the serious or fatal consequences of poor work. In one case on record, a gravely ill Vietnam veteran with fever of undetermined origin was sent to Walter Reed Hospital in Washington, D.C., from another hospital. Walter Reed quickly identified the condition as malaria, but too late to save the patient.

In another case, an 11-year-old boy suffered an extra week of agonizing pain from a hip-joint infection because the hospital was using outmoded laboratory techniques that could not determine the right antibiotic to treat his infection.

There are an estimated 15,000-20,000 clinical laboratories in this country and, when labs in doctors' office are counted, the total probably exceeds 200,000. Before 1967, there was effective regulation of these laboratories in only a few states. The Act brought under control many of

those laboratories doing interstate business. This numbers but 700.

Thus, most persons today still have reason to question whether the results of the laboratory tests ordered by their physicians are accurate. With 3 billion lab tests performed annually, there is cause for alarm.

Recently the Technical Analysis Division (TAD) of the National Bureau of Standards was asked by the Division of Health Evaluation of HEW's Office of the Assistant Secretary for Planning and Evaluation to do one of the largest and most comprehensive surveys of medical laboratories ever undertaken. The NBS study, directed by Peter W. Finkel of TAD, examined some 1,000 laboratories for accuracy and proficiency in three areas: clinical chemistry, hematology and microbiology. A major objective was to compare the performance of those laboratories licensed under the 1967 Act with those not covered or exempted.

Six categories of laboratories were examined. They included federally licensed labs (248), labs run by members of the American Academy of Family Physicians (150), those operated by members of the American Society of Internal Medicine (264),

hospital labs accredited by the Joint Commission on Accreditation of Hospitals (215), Medicare certified hospitals (236) and Medicare independent laboratories (153).

NBS contracted with the Warner-Lambert Pharmaceutical Company to produce test samples in each of the three study areas. The levels of the chemistry and hematology constituents and the time identification of the microbiological samples were known only to Warner-Lambert, 19 reference laboratories and NBS. The samples were shipped to the laboratories which had volunteered to analyze them. Each laboratory's performance was measured on how close it came to the target values established by Warner-Lambert and the reference laboratories. To provide a more valid estimate of each laboratory's capability, two sets of samples were mailed out to each lab, one month apart.

The TAD study found no significant differences for clinical chemistry and hematology among the laboratory groups tested—they were all relatively inaccurate. By this is meant that, for the most part, the results could not be used by a physician with confidence to monitor a patient's condition over an extended period of time.

In the clinical chemistry area, the study group found that laboratories using automated techniques performed better than those using manual methods. "A large percentage of the participating laboratories are using outmoded techniques," the report concluded.

The only clinical chemistry constituent that was analyzed by any of the laboratory groups with sufficient accuracy was cholesterol. Analyses of glucose, urea nitrogen, calcium, uric acid and sodium were not accurate enough to satisfy the criteria of medical utility.

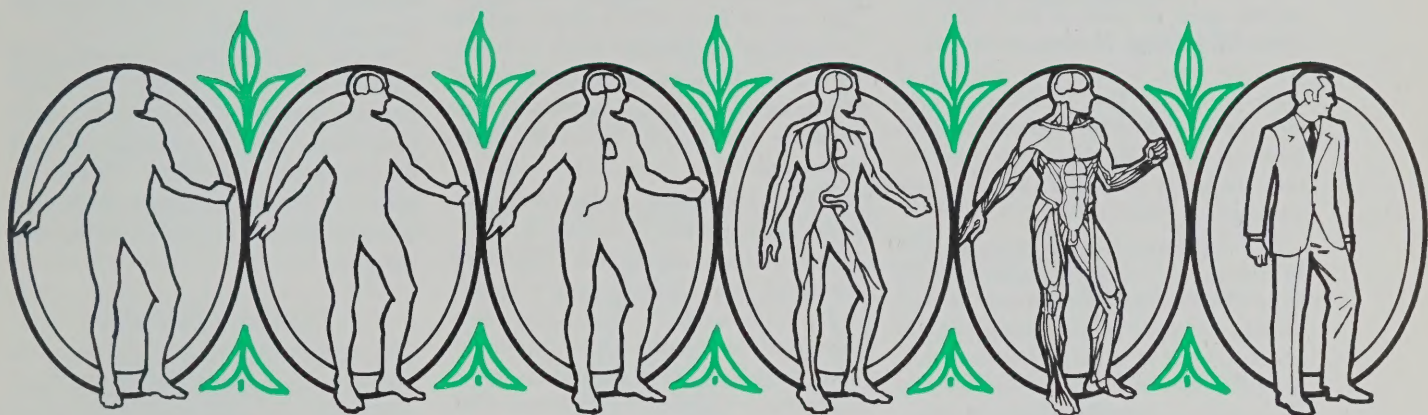
Hematology tests were also too inaccurate to be medically useful. But

continued in page 117



Technicians, like these at the Mount Sinai Hospital and School of Medicine in New York City, perform some 3 billion laboratory tests annually. One federal official estimates one-fourth of these tests are inaccurate. (Photo courtesy of the National Institutes of Health.)

SRM's Help Improve Health Measurements



IMAGINE a person whose medical history was built up over a period of years while living in Boston—a history made up in part by results of tests performed there at a local clinical laboratory. The patient moves to San Francisco, where additional clinical tests are then made at another clinical laboratory. The new tests reveal a much higher cholesterol level than did the test results from Boston. Does this mean the patient may have symptoms of heart disease? Or is it possible that the laboratories used different methods and materials to measure cholesterol so the results are not comparable? The answers to these questions could have life or death implications to the patient.

This hypothetical case points up a predicament of clinical laboratory work in the United States today, according to J. Paul Cali, chief of the Office of Standard Reference Materials at the National Bureau of Standards. Cali explains that both the laboratory in Boston and the one in San Francisco may have been producing highly *precise*—that is, repeatable—results. But unless both laboratories are producing ac-

curate results—results close to the “true” value—there is no way to compare the results directly over time and distance. A comparison of the two results based on precision alone would be risky at best, because either or both of the labs may have their own special, but unknown, errors in their methods.

This problem is magnified by the fact that last year in the United States, upwards of 15,000 clinical laboratories carried out more than 3 billion tests (at a cost to patients of \$6 billion). Yet some medical authorities

estimate that 10 to 25 percent of these test results may have been misleading or of doubtful value to the physician in making a diagnosis or in treating a patient.

This is where the Office of Standard Reference Materials plays a valuable role. At the request of the College of American Pathologists (CAP) and the American Association of Clinical Chemists (AACC), NBS develops and provides selected Standard Reference Materials (SRM's) for clinical chemistry applications. The National Institute of General Medical Sciences of the National Institutes of Health has been providing funds for the research. In addition, NBS is working with some of the nation's best clinical laboratories to establish the accuracy of reference methods for clinical chemistry by developing clinical reference methods.

Standard Reference Materials

SRM's are well-characterized materials produced and certified for purity, composition and/or physical properties. Reference methods are methods of known and proven ac-



Eighteen clinical Standard Reference Materials and one reference method are now available from NBS.

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CLINICAL SRM'S *continued*

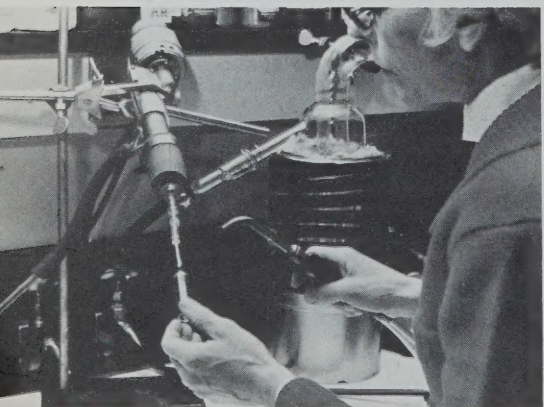
curacy which can be used to determine the error in methods in common use.

Primarily, SRM's are used by manufacturers of secondary standard materials, such as control sera used for daily calibration of automated analyzers, to help assure the quality of their products. The SRM's also provide basepoints that clinical laboratories may use to determine whether tests made on the same materials are accurate.

For instance, the clinical test for bilirubin, a substance that results from the normal breakdown of red blood cells, may be performed 10,000 times a year in a large hospital. Excessive levels of bilirubin are usually diagnostic of certain severe liver conditions. In determining bilirubin levels, the clinical analyst uses a chemical reaction which produces colored products that are measured by a spectrophotometer (an instrument that measures the amount of light absorbed by samples—the amount of light depending on the amount of the colored substance in question). To make this measurement properly, solutions containing known amounts of pure bilirubin are prepared by the clinical chemist. The NBS Standard Reference Material for bilirubin provides a certified high-purity bilirubin for such a purpose.

The SRM can also be used by a

In enzyme field, Dr. Barbara Howell is trying to prepare very pure NADH for use in clinical tests.



large commercial laboratory that produces control materials, or materials of known concentration, which are sold to smaller clinical laboratories. Or a large hospital clinical laboratory might purchase the SRM directly for its preparation of standard solutions. The use of such SRM's helps reduce the margin of possible error in analyses made by clinical laboratories of pharmaceutical firms, hospitals, universities and private research organizations.

NBS involvement in clinical SRM's goes back to the mid-1960's. CAP representatives came to NBS and asked for help in developing a standard for cholesterol. The request was prompted by results of a survey of laboratories which measured the same cholesterol samples. CAP found that some laboratories were in error by as much as 50 percent. At almost the same time, AACC asked for help in finding some of the sources of error in spectrophotometers, the heart of all automated measurements in the clinical laboratory.

By 1967, NBS had issued its first clinical SRM, crystalline cholesterol, 99.4 percent pure, which is widely used today. NBS now has 18 SRM's available for clinical use. In the meantime, AACC and CAP came up with a priority list of many other clinical SRM's that would be valuable to clinical laboratories. Development of those needed with highest priority is now underway by scientists in the Institute for Materials Research under the direction of Dr. Philip D. La Fleur, acting chief of the Analytical Chemistry Division, and Dr. Robert Schaffer, head of the Bioorganic Standards Section and manager of the Division's Clinical Standards Program.

Current efforts in Schaffer's section focus on the field of proteins and enzymes, since nearly 25 percent of the tests performed daily in clinical laboratories are protein and enzyme assays. Standardization of these materials is difficult because they are so complex. At present, Drs. Raymond

McKenzie and William Yap have completed developmental work on a SRM for total protein which uses bovine serum albumin, highly characterized for protein properties and amounts of impurities. McKenzie is working also on a standard for human serum albumin.

In the enzyme field, Drs. Barbara Howell and Sam Margolis are working out criteria for producing very pure reduced nicotinamide adenine dinucleotide (NADH). NADH is used in clinical laboratory tests that monitor blood samples for several enzymes.

Reference Methods

In 1971 NBS developed its first reference method and work has been continuing in this area ever since. The first method provided laboratories with an accurate protocol (a detailed outline of equipment, reagents and procedures) for determining total calcium in serum. (Calcium levels are a measure of thyroid function.) The new method measures the calcium in serum to within 2 percent of the true value. Cooperating with NBS were AACC and the Center for Disease Control (CDC) of the Department of Health, Education, and Welfare.

At least nine different methods are currently in use in clinical laboratories to measure calcium. After comparative testing against results obtained by the reference method, CDC is in the process of recommending that one of the nine should not be used because of its inaccuracies and that four others are in need of improvement. CDC is using the standard reference method to test its 700 Medicare laboratories, and the Food and Drug Administration will rely on use of the method for assuring compliance with its "In Vitro Diagnostic Products" regulations. CAP is now analyzing the data of the calcium measurements in 7000 CAP labs, to ascertain the inaccuracies of the methods used in its labs.

In cooperation with CDC, refer-

ence methods are now being developed for measuring other important salts in body fluids, including sodium, potassium, lithium, magnesium and chloride ions. Working with AACC, NBS and CDC scientists are also at work developing a reference method for determining glucose, which is used as a diagnostic test for many diseases, primarily diabetes.

Another area receiving attention is the measurement of lead in blood. Thousands of blood samples from children are analyzed daily for their lead content as part of the public health programs in the inner city regions of many major metropolitan areas. In New York City alone in a recent year, 100,000 blood tests were made which identified 2,600 cases of lead poisoning in children. The decision to treat children for lead poisoning is often based on these test results.

Last year, Donald A. Becker and La Fleur began work with experts on lead analysis to develop a clinical method for measuring lead in blood based on an atomic absorption technique. With the aid of U.S. Department of Agriculture scientists, they obtained pig blood enriched in lead and with lead analysis experts they assessed the accuracy of some currently available test methods. The basis for evaluating accuracy was provided by the lead analyses performed at NBS by the Isotope Analysis Section of the Analytical Chemistry Division, lead by Dr. I. Lynus Barnes.

This preliminary study revealed that methods now used are as much as 80 percent off the true value in the critical region which determines whether or not a child should be treated for lead poisoning.

Now this team of experts, who work in hospitals and state and Federal clinical laboratories, are trying to develop a protocol for the reference method using a specific atomic absorption technique. The outcome of this work will enable all laboratories to use methods that provide accurate measurements of lead in blood. □

CLINICAL SRM'S CURRENTLY AVAILABLE FROM THE NATIONAL BUREAU OF STANDARDS

SRM No.	SRM Name	Diagnostic Application
911	Cholesterol	Coronary incidence
912	Urea	Kidney malfunction
913	Uric acid	Early stages of gout, kidney failure
914	Creatine	Kidney malfunction
915	Calcium carbonate	Hyperthyroidism
916	Bilirubin	Hepatitis, jaundice
917	D-glucose	Diabetes, liver cirrhosis
918	Potassium chloride	Electrolyte balance, shock or trauma
919	Sodium chloride	Electrolyte balance, shock or trauma
920	Mannitol	Triglycerine determination—blood fat for heart disease
921	Cortisol	Adrenocortical function
922	Tris (hydroxymethyl) aminomethane	Blood acid-base balance
923	Tris (hydroxymethyl) aminomethane hydrochloride	Blood acid-base balance
924	Lithium carbonate	Mental health, manic depression
925	VMA (4-hydroxy-3-methoxy-mandelic acid)	Catecholamine tumors
930a	Glass filters for spectrophotometry	Spectrophotometer calibration
931	Liquid filters for spectrophotometry	Automated spectrophotometer calibration
932	Quartz cuvettes for spectrophotometry	Accurate pathlength for high accuracy spectrophotometry



Thermometric Revolution Brewing



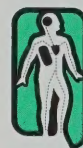
In the operating room, continuous recording of a patient's temperature is facilitated by the use of a tympanic thermometer.

Upper right: Technician demonstrates tympanic thermometer.

If the knife of measurement can be honed to take more and more accurate slices of time (today, billions of seconds; tomorrow, trillions?), how sharp must it be to slice degrees of temperature?

For the National Bureau of Standards' temperature experts, the outlook is: today, thousandths of degrees; tomorrow, millionths—recorded for clinicians, doctors and surgeons within tenths of milliseconds and with measurements possibly taken inside a single biological cell.

Making important contributions to the state of the art in its earliest years, NBS by 1904 stood ready to certify almost any precision ther-



**'They
Don't
Take
Temperature
Like They
Used To'**

monometer used in scientific work and to test on its own special apparatus as many as 600 clinical thermometers at any given temperature in half an hour.

Since then, precision needs in biomedical science have risen phenomenally. Some current demands call for ultrasensitive, rapid or continuous temperature monitoring—vital, for example, in open heart surgery, intensive care units, hospital clinical laboratories and in enzyme data analysis procedures. To help meet the newest needs, NBS is stepping up its work on medically applicable heat sensors.

Looking ahead, Bureau specialists are reaching for hitherto undreamed of levels of refinement in medical thermometry. They aim to provide not only the unprecedented capability that is called for, but also to package this capability in convenient, reliable thermometers—small and very stable—that will give reproducible results for months or years.

All this is a far cry from the dawn of body-temperature monitoring. The first ancient healer touched hand to forehead to see whether the patient was running a fever. Much later, Galileo and his medical disciple, Sanctorius, invented the air thermometer, eventually leading to the fever thermometer that today is sold at the corner drugstore. Voluntary product standards for this familiar mercury-in-glass thermometer have been developed cooperatively by NBS, producers, distributors and users (see NBS PS 39-70).

Among the highlights of current work on temperature-measurement frontiers are the following:

■ NBS is assisting the Food and Drug Administration's Bureau of Radiological Health in its efforts to set safe-radiation standards for diathermy machines and microwave ovens. The Bureau is measuring the temperature distribution in simulated tissues ("phantoms") irradiated by electromagnetic waves. Work with real tissues is planned. To further

this research, a new type of thermometer—liquid crystals using fiber optics—is being developed.

■ NBS is helping upgrade hospital and clinical temperature measurements. The Temperature Section and the Office of Standard Reference Materials at the Bureau are collaborating to supply calibrated, highly specialized liquid-in-glass thermometers geared to new laboratory-approval criteria and inspection standards of the College of American Pathologists and the Joint Commission on Accreditation of Hospitals. This effort is considered a required first step for attaining a better hospital thermometry base.

■ Thermistors—materials that change their electrical resistance as temperature changes—are expected to be star performers in critical-care medicine and clinical chemistry. NBS is working to characterize them in collaboration with thermistor manufacturers, instrument suppliers and hospital centers.

■ Microcalorimetry—a technique for measuring biological fluids' components by the heats of their reactions—has been advanced through improved instrumentation and methods developed collaboratively by the National Institute of General Medical Sciences and NBS thermochemists.

■ Small commercial platinum resistance thermometers are being studied at NBS with regard to stability and reproducibility.

■ A scanning thermal detector, sensitive enough to detect a person entering a room at more than 50 feet, was developed by a father-son/NBS-Naval Ordnance Laboratory team for the National Aeronautics and Space Administration. This instrument is being considered for possible application to patient monitoring in fever situations, as well as for nonmedical applications.

■ Tympanic thermometry—which measures human temperature at the middle ear membrane—is a specialty of an NBS physician-researcher. He is among the leaders in this approach to recording the significant central patterns which monitor the temperature of the heart, the brain and the centers of thermoregulation. The procedure, readily applicable to many patients, is simple to follow and causes a minimum of discomfort.

Recognizing that monitoring patients' temperatures is more reliable and effective when the system used is itself clearly understood and well defined, NBS is readying a Measurement Assurance Program (MAP) for characterization of thermistors and other body-temperature sensors. Through MAP, manufacturers, medical technical societies, clinical laboratories and medical researchers can acquire from NBS a capability for directly calibrating their measuring instruments and insuring the continuing validity of their methods and techniques. □



Jackie A. Wise, chief of the NBS liquid-in-glass calibration laboratory, obtains a thermometer's ice point as part of the procedure for calibrating liquid-in-glass thermometers.

Solving the Lead Paint Problem



Older homes in the center of American cities, small inquisitive children and paint chips that fall from deteriorating walls: These are the ingredients that produce lead-paint poisoning in thousands of American youngsters each year and cause some 200 to die annually.

THE sight is a familiar one for doctors and nurses who staff emergency rooms in hospitals located in America's inner cities. A child, usually between the ages of 1 and 6, is brought in by his parents because he is convulsing. The parents detail a history of loss of appetite, vomiting and constipation. The child has been lethargic and clumsy, they explain.

The child has plumbism—the medical term for what most Americans know as lead poisoning.

Lead poisoning traceable to ingestion of chips and flakes of lead-based paint has received increased public attention in recent years as the magnitude of the problem has become known. This concern was capped with passage of the Lead Based Paint Poisoning Prevention Act by Congress in 1971. The Act gave the Department of Housing and Urban Development (HUD) primary responsibility for research and demonstration activities relating to lead poisoning. HUD, in turn, contracted with the National Bureau of Standards for technical and scientific expertise.

Although an estimated 200 children die each year from lead poisoning and another 12,000 to 16,000 have significant enough elevations of lead in their blood to cause blindness,

mental retardation and other severe consequences, this is only the tip of the iceberg.

"The effects of moderate lead absorption are not known, but medical researchers are becoming increasingly concerned that permanent learning and intelligence dysfunctions may result from even low-lead exposures," Harvey W. Berger, program manager for the lead-based paint poisoning program in the NBS Center for Building Technology, told a recent conference.

The NBS effort is centered around the problem of lead poisoning caused by children chewing on paint chips, window sills, baseboards and other surfaces covered with lead-based paint. This paint was used extensively in homes before the 1940's and is still present, especially in deteriorating houses in center city areas.

There are three aspects to the NBS lead-based paint program: an estimation of the size of the problem, evaluation of methods for detecting lead in paint and the identification and evaluation of techniques for eliminating the lead paint hazard in housing.

A team of NBS engineers, chemists, mathematicians and other professionals are working on the project under HUD sponsorship and funding.

Magnitude

There are 17 million children aged 6 or less who live in this country's urban areas. NBS estimates 2½ million live in dilapidated or deteriorating housing and that more than 500,000 of these children have elevated levels of lead in their bodies. But the figure is imprecise and may be a serious underestimation.

Consequently, the Bureau is contracting with the Allegheny County (Penn.) Health Department, which includes Pittsburgh, for a survey of 4,000 randomly selected dwelling units and the screening of children living in those dwellings. All children 6 years of age and under living in these units will be examined for blood-lead levels.

Berger says the survey "should vastly improve our estimates of the extent of the lead poisoning problem in terms of both the numbers of children involved and the contributions of the housing environment."

One result of the survey is expected to be a manual prepared by NBS for use by local health and housing agencies in estimating the size of the problem in their communities. The manual will explain survey techniques, contain a computer program for analyzing survey



data and train survey personnel to use lead paint detectors. NBS also hopes to develop a more precise standard for measuring blood-lead levels. Most measurement tools now are based on soluble lead compounds added to animal blood. Chemists in the Analytical Chemistry Division of NBS are developing a standard based on blood taken from pigs that have been fed lead compounds. This protein-bound blood lead standard is expected to be biochemically representative of the blood samples obtained from children.

Detection

NBS has evaluated a number of techniques for analyzing lead in paint. These have included atomic absorption, polarography, anodic stripping and colorimetric spectrophotometry. They are routinely accurate and only take minutes to perform. But they all require hours of treatment with acids and high temperatures to prepare for analysis. The time and cost involved make these methods unacceptable for mass screening.

NBS has also evaluated portable X-ray fluorescence detectors that are becoming popular with local housing authorities. NBS has found these instruments accurate to a level of 2

milligrams of lead per square centimeter. But they are inadequate at lower lead levels which may constitute serious health hazards.

In addition, HUD has recently released a Request for Proposal (RFP) which will encourage development of quick, simple and reliable detection methods. NBS will monitor contracts resulting from the RFP and will evaluate the efficiency of new detection devices and systems.

Elimination

The ultimate solution to the lead paint poisoning problem lies in preventing access to the source. With present knowledge and techniques it costs approximately \$2,500 to de-lead a single residence. There are 30 million homes constructed before 1940, many of them finished with lead-based paints. To de-lead these would cost an estimated \$75 billion.

HUD and NBS are now preparing a field demonstration program that will encompass a total of 250 homes in four cities: Washington, D.C., Atlanta, Cincinnati and Los Angeles. Some 20 techniques for de-leading homes will be tested in public housing complexes or in Federal Housing Authority acquired properties. NBS will monitor the program for technical performance and will report to HUD

on the ultimate cost effectiveness of the techniques.

Long-Range

NBS will continue to work with HUD to identify and evaluate new methods for removing lead-based paint from the Nation's older homes. As one example, NBS is hopeful that a bad-tasting coating recently developed by industry that can be applied over walls covered with lead-based paint will be effective in discouraging children from eating paint chips.

NBS will continue to serve as a resource for HUD as well as the Department of Health, Education, and Welfare, the Environmental Protection Agency and the Consumer Product Safety Commission in attempting to define the extent of the hazard. Part of NBS' function will be to collect documents and make them available to local governments and lead paint control programs throughout the country.

Hopefully, through cooperative research efforts by numerous Federal, State and local agencies, and the implementation of housing and health programs deriving from that research, the incidence of a child being rushed to an emergency room because of lead poisoning will become a medical rarity. □

The NBS Reactor:



A patient at Walter Reed Army Medical Center, who has been treated with radioactive fluorine-18, is scanned for bone cancer.

Tool for Health Research

INSIDE one of the buildings at the National Bureau of Standards—set apart from the others—it's as bright as daylight. Mercury vapor lamps cast a shadowless blue light over a large cylindrical structure around which are crowded banks of scientific devices and instruments.

Towering nearly three stories high, the cylinder's walls of steel, concrete and lead house a complex assembly undergoing the most powerful sustained process man can control. The process is atomic fission and the giant cylinder is an atomic reactor.

The NBS reactor is not, however, one of those built primarily to generate power. Its function, rather, is to serve as a research tool and it is one of the more sophisticated and versatile research reactors now existing. Because of the reactor's unique design, the high-intensity neutron beams it provides and its unusual and extensive irradiation facilities, it can, and does, serve a large number of scientists and engineers in a broad range of projects both within and outside the Bureau.

It is especially suited to the study of the constituents of materials and the production of radioisotopes. Last year, for example, nearly 50,000 specimens were activated and analyzed at the reactor.

Major Health Programs

Many of the reactor programs relate directly to health. Here is a short summary of eight of the more significant ones. More will be said about three of them later in the article.

1. *Contaminants in foods.* This program involves the analysis for trace elements—elements present in very minute amounts—in practically all types of foods consumed in the United States today.

2. *Purity of drugs.* Numerous drugs are being analyzed to ensure quality and detect impurities. One result was the exclusion of certain antibiotics imported from abroad.

3. *Harmful materials in consumer products.* The products examined include (a) laundry aids such as all kinds of detergents, including pre-soakers and enzyme detergents, analyzed for arsenic and antimony, (b) cosmetics, analyzed for mercury and (c) deodorants, analyzed for irritants.

4. *Role of trace elements in medicine.* Several medical centers are using the reactor to study how the presence of certain trace elements (zinc, manganese, iron, magnesium, cadmium) are related to health and disease.

5. *Clinical and biological Standard Reference Materials (SRM's).* SRM's currently being analyzed by the Activation Analysis Section range from standards for calibrating clinical laboratory instruments to trace element standards like SRM 1571, Orchard Leaves, which is used in agricultural and pollution studies.

6. *Oxygen in human tissues.* The program aims to measure accurately the amount and distribution of oxygen in brain cells, believed a critical factor in several brain disorders.

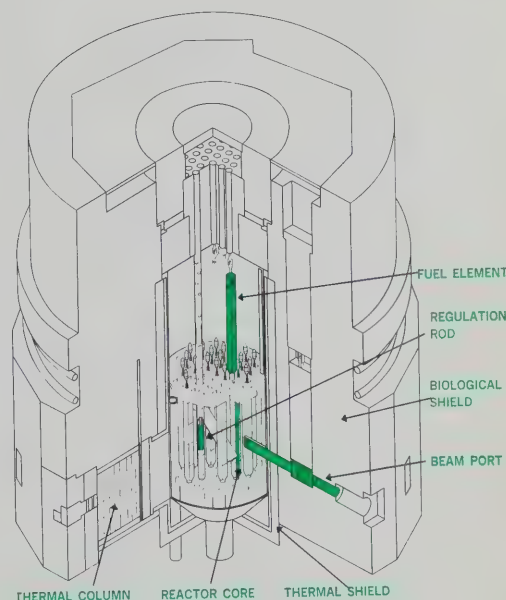
7. *Structure of dental materials.* Several investigative methods, including neutron diffraction, are being used to determine the structure of tooth materials and materials for dental fillings.

8. *Radioisotopes for medicine.* Radioisotopes have been produced for most major Washington-area medical centers. Fluorine-18, used to detect bone cancer, was produced in

large quantity over a 3-year period.

Neutron Activation Analysis

This technique, used in most of the above programs, is one of the most powerful in the reactor's versatile kit. The sample to be analyzed is put into the reactor where it is bombarded by the dense neutron streams coursing through the hot core until constituents in the sample become



Cutaway of NBS reactor.

radioactive. When this happens, the constituents start giving off characteristic rays. These rays can be measured to determine the type and amount of the constituent in the sample.

Neutron activation analysis has the remarkable property that the specimen, once it is irradiated, can be processed in all sorts of ways—mechanically manipulated, heated,

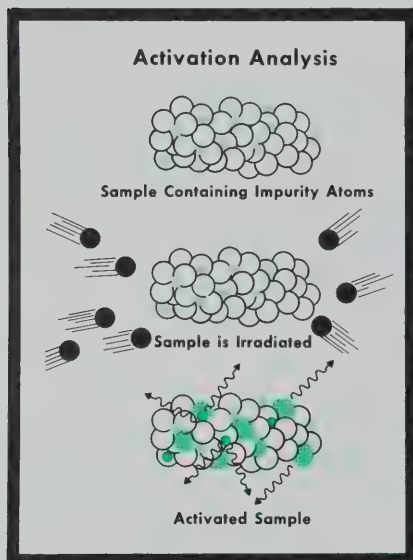
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REACTOR *continued*

mixed with strong chemical reagents—without affecting the final result. It does not matter if the specimen is mixed with materials containing considerable amounts of the very same element whose concentration we are trying to measure. It is also a non-destructive process since it can work without chemical separation or with samples so small their removal does not affect the parent system.

Contaminants in Foods

It has been suspected that contaminants in foods—mercury, arsenic and selenium, for example—can be harmful even in relatively small



doses. The heavier metals in general have been shown to be highly toxic. We also know that they accumulate in the body and can reach dangerous levels over a period of years. We needed to find out, therefore, just what amounts of the dangerous or potentially dangerous substances are taken in with our diet.

The Food and Drug Administration (FDA) has conducted an extensive program of analyzing common foods using the NBS reactor, beginning with a study of mercury in fish. Now, total diets are being analyzed, including 126 food types, for many contaminants.

Effects of the contaminants found in foods are studied by feeding controlled amounts of the contaminants to animals and then examining samples of the animals' tissues.

Oxygen in Human Tissues

While the reactor is being used to analyze materials that touch our everyday lives, scientists in the NBS activation analysis group are also using it to expand the frontiers of medicine. Several lines of evidence suggest that the amount and distribution of oxygen in human tissues may be critical for certain diseases. A low level of oxygen in the brain, for instance, has been linked with mental disorders. And certain types of tumors are characterized by either too much or too little oxygen.

But until the "nuclear track technique" was developed, it was difficult to measure oxygen in tissues. It happens that ordinary oxygen (oxygen-16) is not easily measurable at the trace level, but oxygen-17 is. Therefore, the first step is to replace a fraction of the oxygen in the body by oxygen-17 and samples, say from the brain, are put into the reactor mounted on a film of glass or plastic. When the oxygen-17 becomes radioactive, it ejects alpha particles that produce tracks in the film, tracks that look similar, though of course smaller, to the tail of a comet. By measuring and analyzing these tracks, and counting them, one can tell accurately the amount and location of oxygen in the tissue being studied. This, in brief, is the method used in a program carried out by NBS in collaboration with the Weizmann Institute of Science in Israel.

Detecting Bone Cancer

Fluorine-18, known as F-18 for short, is an extremely useful radioisotope for imaging bones and revealing abnormalities in them. Fluorine is selectively absorbed by bone; that is, the fluorine tends to settle in bones rather than in other tissues. And where the bone is diseased, even very

slightly, it is absorbed to an even greater degree. With F-18, tumors can be detected at a much earlier stage than is possible with x-rays. Moreover, if the affected bone cells should start to migrate, carrying the cancer to other parts of the body, this important fact can also be detected. Results of repeated F-18 scans have a high consistency, so that one can follow the effects of a given kind of treatment from day to day, or more often, if necessary.

F-18 does, however, have some technical drawbacks. In one day, its radioactivity drops by more than 99.9 percent, which means that F-18 cannot be stored very long before use. Also, rather sophisticated reactors are needed to produce F-18 and few of these are available.

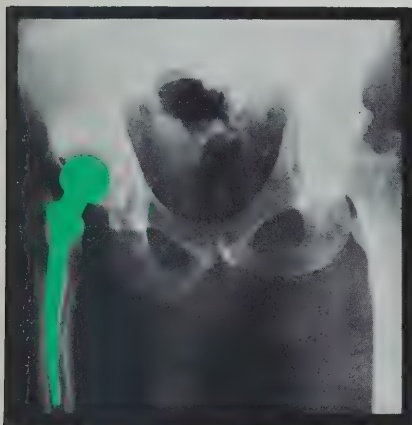
Medical researchers are therefore looking hard for a radioisotope that overcomes these difficulties. A promising candidate is technetium-99m which has been in use for brain and other scans. It was shown at Upstate Medical Center in Rochester, N.Y., that technetium can be selectively absorbed by bone when it is compounded with polyphosphate.

In this work, F-18 itself is playing a vital part as a standard of comparison for judging the accuracy and consistency of different ways of preparing the technetium.

Other Programs

The research described is only a small part of the health-related programs of the NBS reactor. These, in turn, are a small part of the reactor's total activities. One should at least mention the projects concerned with criminal detection (many analyses are made for the FBI and other law enforcement agencies) and with contaminants in air and water. Then there are extensive programs in the physical sciences and engineering, dealing with such subjects as minerals (including moon rocks), magnetic solids, semiconductor glasses, simple liquids, liquid metals and phase transitions in solids. □

Getting it Together Polymerically



*X-ray of a
restored hip joint.*

forms only a mechanical attachment to the bone and prostheses and is, therefore, not an adhesive.

In certain cases, poly(methyl methacrylate), or variations of it, can stabilize devices for repairing fractures, fill voids in a bone, form replacements for skull defects and even act as a splinting material to treat instability of the spine.

In the last 4 years in the United States—and earlier in Europe—orthopedic surgeons have been successfully applying the cement. But up to this time, the material and its reactions during polymerization (setting) have not been well characterized. Such a characterization could help surgeons optimize control over processes like joint replacement.

The Research Project

NBS chemist Dr. Gerhard Brauer and physicist George Dickson have long been familiar with the main ingredient of this cement through their work in the Dental Research Section. By putting their knowledge of the material together with the expertise of orthopedic surgeon Dr. Stephen Haas of George Washington University Medical Center, the researchers have come up with a characterization that may be just what the doctor ordered. An important goal of the project is the production of information which would be both comprehensible and useful to the practicing surgeon, as well as valid and meaningful to basic scientists.

The research has been directed toward a determination of the properties of the cement as it is prepared and used in the surgical procedure. Specifically, the NBS study has involved characterization of the chemical, physical and mechanical properties of the polymerized substance and an attempt to define those factors involving the use of this material—factors controllable by the surgeon—which may affect the performance of the cement.

In addition, an effort is being made to define factors which may be potential causes for malfunctioning and to improve safety and reliability. This should provide the industry and those involved in clinical work with information as yet unavailable.

The material currently in use in this country was first introduced to the orthopedic community in England. It consists of a plastic bag of sterile powder and a glass vial of sterile liquid. The bag contains powdered poly(methyl methacrylate), methyl methacrylate-styrene copolymer, an initiator, and may include barium sulfate for radiopaqueness. The vial contains monomer, accelerator and inhibitor. Research results indicate that the method of preparing the mix can influence dough time (time from initial contact of powder and liquid until cement is ready for insertion), handling time (period between dough and setting times), setting time and peak temperature of polymerization.

Additional Activities

In an effort similar to that which over the years has produced specified quality materials for dentistry, the researchers are collaborating with scientists and orthopedic surgeons on the American Society for Testing and Materials F-4 Committee to formulate standards for poly(methyl methacrylate)-based materials used in total hip joint replacement and neurosurgical applications. Characterization of the polyethylene component of hip and knee prostheses is also under consideration. □

NOT long ago people with damaged hip joints had to accept the fact that they would not walk again. Doctors had tried various methods of replacing joints, but until recently, the problem continued to stymie the surgeons. Then a material that had been around for 30 years—in such widely different products as road signs and dentures—was combined with other ingredients to make a bone cement.

The cement, called poly(methyl methacrylate), is “made” in the operating room by the surgeon who mixes a liquid and powder together to get a doughy mass. At the right moment he packs this dough into a prepared bone and positions a metal artificial part (prosthesis) to replace the removed, damaged part of the bone. A plastic cup is similarly attached to the pelvis, and the new joint is complete.

The cement serves almost as a mortar to steady and cushion artificial parts—for the hip and other joints as well. Though it may be described as a filler and a binder, it

New Computer Language Standard Aids Medicine



A Spanish-speaking woman comes to the Harvard Street Clinic in Dorchester, Mass., for a physical examination. Before she is seen by a doctor, a nurse seats her before a television screen and a keyboard resembling a typewriter. The nurse punches a few keys and a question in Puerto Rican Spanish lights up on the screen. The woman is asked a series of questions about the general state of her health. She responds by pushing the appropriate multiple-choice keys on the keyboard and additional questions in Spanish appear, asking for more detail. The woman responds and still more questions appear. The process is repeated until the woman has given the machine her complete medical history.

When the medical history is finished, the woman is ready to be seen by a doctor who has reviewed a computer printout, in English, of the information given to the machine by the woman. With the medical history in hand, the doctor begins a thorough examination of the patient.

AT the Harvard Street Clinic, this scenario is repeated many times a week, sometimes in Spanish, but also in English and Haitian French. It is one of the most dramatic applications of a unique computer programming language finding wide use in the medical profession for processing large quantities of medical information. The language is called MUMPS (an acronym for *Massachusetts General Hospital Utility Multi-Programming System*).

This highly effective computer programming language, specifically tailored for low cost computers, is used in more than 125 medical applications, ranging from automated patient history taking, to maintaining ambulatory care records, to x-ray reporting. From its initial beginning at one hospital in 1967, MUMPS has spread to more than 100 medical institutions in the United States and is being used by health care professionals on every continent of the world as a tool for improving health care delivery. Eventually, the language could be used in thousands of hospitals, research institutions, group medical practices and by individual physicians to store and retrieve data on patients, research and administrative functions.

Standard Development

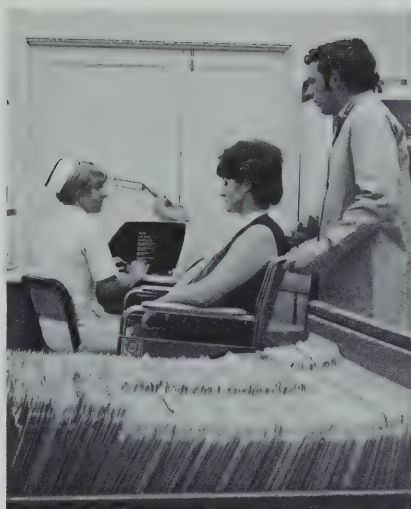
MUMPS was originally developed 7 years ago by physicians and computer scientists at the Massachusetts General Hospital in response to the need for a means of handling the increasing volume of health care information and the growing shortage of trained medical personnel capable of dealing with it. Since that time, the Department of Health, Education, and Welfare (HEW) has sponsored a multimillion dollar research effort geared to development of the MUMPS computing language and operating system and the production of many hundreds of MUMPS application programs. A recent part of

this effort has been directed to the development of additional capabilities within the MUMPS language and a standard specification for the language. HEW asked the help of the Institute for Computer Sciences and Technology (ICST) at the National Bureau of Standards, since it had considerable experience in aiding the standardization of other computer programming languages, including COBOL and FORTRAN. Since 1965 ICST has been responsible for standardizing computer languages used by the Federal government.

The last year has seen an intensive standardization effort involving HEW's Donald R. Barnes, ICST's Joseph T. O'Neill and Martin E. Johnson and representatives from each of the MUMPS language sponsoring institutions. As a result of this effort, a proposed standard has been developed which defines MUMPS in a single set of language specifications incorporating the best features from among each of the eight variations, or dialects, that had emerged. The standardization effort is geared to guaranteeing that MUMPS programs are easily transferred to a wider variety of users. Because of the interest in the development of a standard, the current proposal was arrived at within the space of a single year.

Answer to Problems

MUMPS has turned out to be an answer to many of the problems confronting health care personnel who wish to use computers for medical information processing. Many systems require a large capital investment for computer equipment and trained personnel to operate it. These two factors have put many computer systems out of reach of all but the largest hospitals and medical centers. MUMPS, however, can be used on relatively small, inexpensive machines. The language is comparatively easy to use, allowing new MUMPS



At Marlboro Hospital, Marlboro, Mass., MUMPS is used for admissions, scheduling and making active patient data readily accessible from a variety of sources. Above, a nurse seated at the computer console updates a patient's record.

applications to be quickly developed and tailored to individual needs. One of the greatest advantages to a programmer wishing to use the MUMPS language is its ability to be used in a "conversational" mode. This capability allows a programmer to correct his errors immediately while he is developing his program rather than going through the frustrating delays of repeatedly submitting his program to the machine.

Like other computer systems used in delivery of health services, MUMPS saves time for the physician. But it also has an unexpected benefit: patients frequently tend to be more honest and open about their past with the computer than with a doctor. MUMPS also enables health professionals to cope more efficiently with patient files. A patient's medical file contains literally hundreds of pieces of information relating to his past history, current symptoms, results of tests and drug treatment. One of the principal benefits of MUMPS is the language's ability to construct a single integrated file of patient medical data.

Denver General Hospital and Denver's Neighborhood Health Program, for example, use MUMPS to keep files for some 110,000 patients. This system has cut down on the number of files that are misplaced and lost as a result of transferring them from file rooms to various locations in the hospitals and clinics. Like many other systems, MUMPS can be employed simultaneously (time-shared) by several users. This is of special value for Denver General since the Neighborhood Health Program has seven clinics dispersed throughout the city.

MUMPS is also valuable in processing clinical laboratory information resulting from specimen analysis and in preparation of worksheets and laboratory test reports. Clinical data management was the initial MUMPS application pioneered by the physicians at Massachusetts General Hospital.

Increased Use

The standardization of MUMPS should lead not only to increased use of MUMPS in medicine but in non-medical fields as well. ICST's O'Neill points out that the Bureau receives new requests for information about MUMPS on a daily basis. Moreover, MUMPS machines are being installed in over a dozen countries, he says, primarily for medical applications, but also for banking, inventory control and parts management, film library maintenance, hotel administration and the keeping of real property records.

Summing up, Dr. Bruce Waxman, Director of HEW's Health Care Information Systems and Technology Division, says "Like many other pivotal technological developments, the MUMPS language has enabled a large spectrum of important health services to become available to this Nation on a time schedule and with an economy of effort that could not have been possible otherwise." □



AMERICA's system for collecting and transfusing blood is ailing.

The Nation's blood banks have been criticized for lack of coordination and duplication of efforts. Located in one city, for example, may be a Red Cross blood donor center, several hospital blood banks and one or more commercial firms that pay persons to donate blood. There is often little communication or cooperation among the various centers.

This duplication boosts the costs of collection, processing and storage. It also causes stockpiling problems and leads to poor management. In this situation the chances that a unit of blood will become outdated before it can be used are increased greatly.

Added to the organizational problems is the risk of acquiring hepatitis through blood transfusion. A patient today stands a one-in-fifteen

chance of contracting hepatitis by transfusion. In 1971 some 3,000 Americans died from complications related to transfusions; a substantially larger number had to be hospitalized or endure long convalescences due to blood transfusions.

Task Force Appointed

Problems with the blood banking system were so acute that, in 1972, President Nixon appointed a Task Force to recommend remedial action.

A prime responsibility for the effort rested with the Department of Health, Education, and Welfare (HEW). In that connection, HEW's Assistant Secretary for Planning and Evaluation asked the National Bureau of Standards' Health Systems Group to perform cost analyses of the present blood banking system and develop feasible alternatives.

That report to HEW has helped to reshape thinking and policy making in the Nation's blood banking system. Prepared by a research team directed by Ted R. Miller of the Technical Analysis Division in the NBS Institute for Applied Technology, the report produced two major conclusions:

1. Contrary to previous belief, a high percentage of eligible Americans volunteer to give blood at least once. But many of these donors refuse to become repeat givers for a variety of reasons.

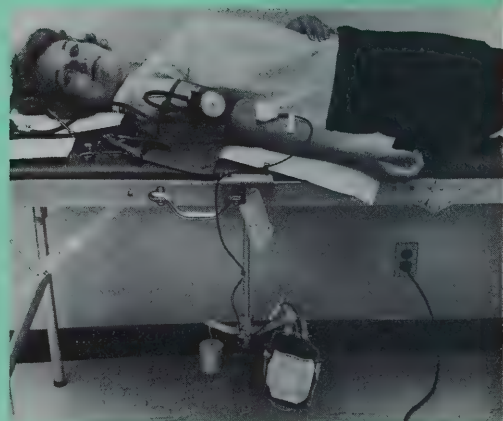
2. In estimating the cost of a blood transfusion, the indirect costs of disease and hospitalization must be figured, as well as the direct costs of collecting, storing and transfusing.

The NBS team found that operators of blood banking systems stress recruitment of new donors under the belief that only 2 to 4 percent of eligible donors in any population group give blood. "These claims and inferences prove to be incorrect," Miller states in a summary of his group's report.

The NBS survey showed 8 to 10 percent of eligible donors give blood in a 1-year period. And, over a 10-year period, 30 percent of those eligible have given blood.

What the NBS researchers did find was a high turnover rate, with many donors giving only once and refusing to give again. Blood program managers were found to "severely underestimate" the adverse reaction rate among donors and generally have

Study on Blood Banking Bears Interest



poor follow-up systems to catch these reactions.

Interviews with 100 NBS employees showed more than a quarter of those who gave blood stopped because of adverse reactions. Another quarter stopped because of medical ineligibility, often caused by such transient conditions as anemia. Miller said individuals in the latter group were "afraid" to try donating again because of negative reactions produced by being told their blood wasn't wanted.

Common adverse reactions include weakness, dizziness, fainting, pain or swelling. These were precipitated—or aggravated—by inadequately trained personnel who leave painful bruises when searching for veins, by an anticoagulant used to sterilize needles that stings severely and by the amount of blood taken from donors.

"There is normally no follow-up with donors to answer questions they may have, get feedback on adverse reaction or reduce the trauma of medical disqualification," the NBS group found. "Attempts to reduce donor reaction would probably have a higher payoff than increased recruitment effort," they concluded.

New Cost Concept

The cost of a unit of blood is generally thought to be the fee the recipient pays for whole blood and its administration by a health professional. But the NBS team included such indirect costs as an extra day of pre-operative care because blood was not available on the day scheduled for the operation, and the cost of continued treatment for post-transfusion reactions.

"The total cost of a unit of blood was estimated as the sum of indirect costs and direct costs, whether or not the payment of such costs was subsidized," Miller noted.

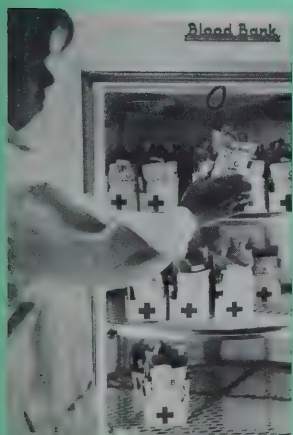
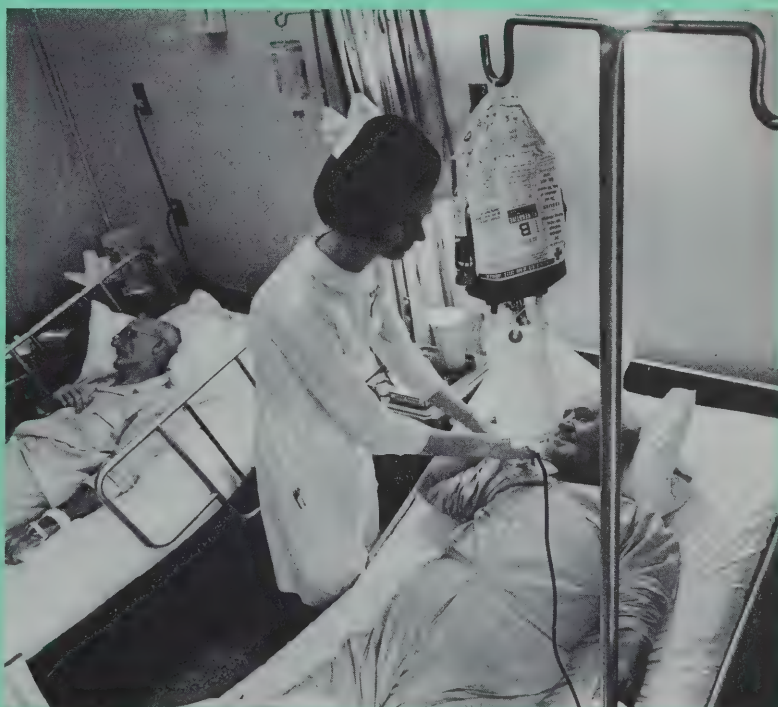
This more comprehensive costing method was applied to eight alternatives to the present blood banking system, the most attractive of which were:

- Conversion to a frozen red blood cell storage system.
- Emphasis on donor retention and frequent review of the physician's decision to order transfusions.
- Extending the shelf life of blood from 21 to 28 days plus regionalization of collection efforts and adequate follow-up.

Policy Options

The NBS team did not attempt to select the best of the three alternatives, stating that the choice should be left as a policy decision for HEW. They did find that a frozen red cell system, although more expensive, would carry the lowest risk of disease and death. The physician-review system would hopefully reduce the number of transfusions—and the cost of the system. And the regionalization system would be the easiest and least costly to implement.

The 109-page NBS report has had a favorable impact on the medical community. Among other things: The HEW Task Force used the NBS cost analysis framework to evaluate its recommended system; the American National Red Cross is converting much of its operation to a frozen red cell system and has adopted the cost analysis framework for long-range planning; *Transfusion*, the journal of the American Association of Blood Banks, expects to publish the section of the report dealing with donor eligibility and the Swedish National Blood System is using the NBS cost analysis framework. □



NBS Marks 55 Years of



Dental Research



Correlating research findings with clinical practice is the job of technician Richard Manuszewski (left) and ADA Research Associate Dr. Nelson W. Rupp as they examine patient in NBS dental clinic.

NEXT time you visit your dentist, look around. Chances are the drill he uses is directly descended from one conceived and developed at the National Bureau of Standards 20 years ago.

The water turbine, contra-angle, high-speed handpiece, forerunner of today's air-driven dental drill, is probably the most important advancement in dental equipment in this century. It is only one item on an impressive list of dental equipment, materials, standards and specifications that have resulted from a collaborative research program involving NBS, the American Dental Association (ADA), the Federal dental services and other government agencies. Close contact with the dental manufacturing industry has been a characteristic feature of the program.

The program is under the leadership of Dr. James Cassel, Chief of the NBS Dental Research Section, and Dr. Walter Brown, Director of the ADA Research Unit at NBS. The emphasis is on development of improved dental restorative materials, equipment and preventive dentistry techniques. A fully equipped dental clinic on the NBS grounds at Gaithersburg, Maryland, makes it possible to correlate many laboratory findings with clinical practice. Financial support for this multidisciplinary program also comes from the National Institute of Dental Research of the National Institutes of Health and the Army Medical Research and Development Command.

Aid to Army

The dental materials program at NBS began in 1919 when the U.S.

Army Dental Corps came to the Bureau for help in establishing standards for dental amalgams (used for fillings) of improved quality and durability. The first standard for amalgam alloy, completed in 1926, was done with such thoroughness that it has only undergone one major revision since.

Shortly after this standard was issued, NBS' long-standing association with the ADA began in 1928. Under the direction of Dr. Wilmer Souder, founder of the Dental Research Section and its guiding force until 1945, the 1930's witnessed a great expansion in the research program. Emphasis was placed on basic research in the physical and chemical reactions of many materials. The period was productive and resulted in an improved understanding of practically all materials used in restorative dentistry.

Milestones among the many accomplishments of the section include:

- Standards were developed for dental materials based on measurement of properties of dental significance. These were developed in collaboration with the ADA. The ADA publishes a biennially revised guide to dental materials and devices which lists those products that comply with ADA specifications.

- The panoramic dental x-ray machine was developed in the 50's. This unique machine produces an x-ray picture of the entire dental arch with the supporting bone structure. It does this with one large film, thus replacing the complete mouth examination of 14-20 pictures formerly required.

- The high-speed handpiece was developed in 1953. Within a year of its development at NBS, the technology had been made available to industry. The drill makes the work of cavity preparation and tooth reduction faster and easier for the dentist. More important, it is much more comfortable to the patient.

■ Spherical particle alloy for use in amalgam was developed in 1963. It is estimated that the alloy is now used for one third of all amalgams. The alloy allows amalgam properties to be controlled by suitable particle size distribution.

■ A new more durable, tooth cement, based on *o*-ethoxybenzoic acid (EBA) used in cementing crowns and bridges, was developed in 1964.

Composites Take Hold

In addition to these highlights spanning many years, one of the most dramatic developments in modern day dental research is the synthesis of direct-filling composite restorative materials. These are composed of an organic resin and inorganic reinforcing fillers. The basic research leading up to this development began in 1956. Late in 1957, Dr. Rafael Bowen, an ADA research associate chemist and dentist, synthesized a substance, BIS-GMA, that made composites feasible. Composites were formulated, evaluated and then publicized in dental journals.

Composites quickly established a

place in the practice of dentistry because they were more durable and did not discolor as readily as older direct filling silicate cements. Since the composites are used on front teeth for esthetic as well as health reasons, these are important properties.

There are now over 12 brands of dental composite restorative materials sold in the United States, all based on the original formulation developed in the Dental Research Section. More than half of all esthetic restorations currently done are of this type of material. In view of such widespread use, much of the research efforts in this project in the last few years have been attempts to perfect, through synthesis and evaluation tests, the various ingredients in the formulations.

An Ounce of Prevention

Today, the emphasis in dental practice is on prevention, so ADA research associate Bowen, NBS chemist Dr. Joseph Antonucci and ADA chemist Harold Argentar are turning their attention to development of

materials for preventive dentistry. One promising approach involves the sealing of the so-called "pits and fissures" of teeth with a hardenable polymer resin. Pits and fissures, natural defects in about half of all posterior teeth, act as breeding grounds for decay.

The success of a sealing procedure depends on the stability of a surface adhesive bond between the sealing polymer and the tooth enamel surface. In preliminary studies carried on by the National Institute of Dental Research at NIH, children whose teeth were sealed with the resin had about 66 percent fewer cavities than a group of nontreated children. New research is geared to developing better agents that will attach more effectively to the tooth mineral.

Other current research efforts are directed toward improved topical fluoride treatments, improved tooth "etching" procedures and the development of a better understanding of the physicochemical basis of the mineralization and demineralization that occurs in dental caries, periodontal disease and other calcium-involved phenomena. □

CLINICAL LABS *continued*

some of the largest discrepancies were found in the microbiology area where common organisms that cause pneumonia, strep throat, food poisoning and other diseases were not always identified by the laboratories.

Federally regulated labs were rated best, but even here 7.6 percent of the identifications were incorrect. For all other laboratories, the rate of error averaged 19.9 percent. Medicare hospitals and physicians' office labs were the worst performers. "Even a 7.6 percent misidentification rate is not satisfactory because the organisms selected (for testing) are common and should be easily identifiable" was the opinion of the Advisory Committee which guided the scientific aspects of the study.

In offering its general conclusions,

the report noted that high-volume laboratories—which frequently use automated test equipment—may be more proficient than smaller laboratories, such as in doctors' offices and small hospitals, where there is more manual testing.

And while the Center for Disease Control's proficiency testing has significantly improved the performance of federally regulated laboratories in microbiology testing, this was not the case with hematology and clinical chemistry testing, the NBS group reported.

"It is particularly important to improve the effectiveness of these programs because the interlaboratory consistency of study participants with respect to clinical chemistry and hematology was too often insufficient to support monitoring of an individ-

ual's constituent concentrations over time. It appears that poor selection of techniques is an important factor in the low rate of acceptability of laboratory determinations," the report concluded.

The NBS group recommended that:

■ Participation in a federally approved microbiology proficiency testing program should be a legislative requirement for all laboratories conducting this type of testing, whether they are intra- or interstate firms.

■ A better design for proficiency testing programs in clinical chemistry and hematology be developed.

■ Federal and State governments, professional societies and accreditation agencies make a concerted effort to get laboratories to use the best testing methods available. □

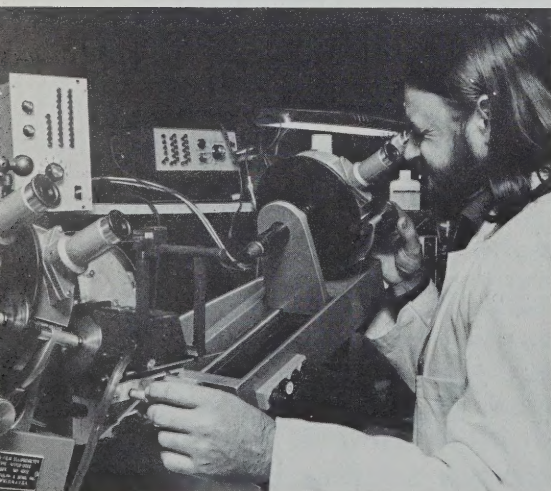
Protein Adsorption Applied to



Blood Compatibility

THOUSANDS of people are alive today thanks to the progress made by the medical and scientific professions in simulating and replacing defective body parts with man-made devices. At present, some 45,000 artificial heart valves and 100,000 artificial arteries have been implanted and at least 15,000 people a year with chronic kidney disease are kept alive by artificial kidney machines.

Despite these successes, kidney machines and synthetic implants are far from perfect. One of the most serious problems associated with these devices is blood clotting and anticoagulant drugs are usually required to prevent such clotting. Clotting on the surface of a heart valve, for instance, can impair its function or cause it to fail.



NBS physicist Carl A. Fenstermaker uses an ellipsometer to learn more about behavior of proteins on synthetic surfaces.

In the case of kidney machines, a patient's blood is passed through a membrane in the machine which "filters out" poisonous wastes that cannot be handled by the patient's kidney. The purified blood is then returned to the patient. Blood proteins bound physically or chemically to the membrane (protein adsorption) can rob the patient of essential blood components as well as decrease the efficiency of the device.

For such reasons, scientists and medical researchers are interested in finding out what causes blood clotting and protein adsorption on synthetic surfaces. One aspect of the clotting process which may provide insight into synthetic implant failure is being studied by chemists at the National Bureau of Standards. The research is funded in part by the National Heart and Lung Institute of the National Institutes of Health.

Complex Process

"Blood clotting is an extremely complex process made up of many steps," emphasizes Dr. Robert Stromberg, deputy chief of the Polymers Division. "We're not trying to solve the clotting process or even trying to develop new materials for implants. What we are trying to do is isolate and understand certain interactions that occur between blood proteins and synthetic surfaces.

The NBS researchers approached the problem by looking at changes in the shape or conformation of proteins that might occur when they are adsorbed on synthetic surfaces. Such changes are of interest since many scientists believe they lead to alterations in the biological activity of the proteins, which may be related to initiation of the clotting process.

Using infrared spectroscopy, Dr. Bruce W. Morrissey and Stromberg followed changes in conformation of three proteins after they were adsorbed onto a silica surface by measuring the number of points at which the large protein molecules contact

the surface. The proteins were fibrinogen and prothrombin, two substances involved in the clotting process, and serum albumin, the component of highest concentration in blood plasma. Their results indicate that the conformation of all three proteins remains relatively unchanged from their shape in solution after they are adsorbed on the silica surface, regardless of the amount adsorbed or the time elapsed. Similar investigations on other proteins and surfaces are now underway which show that changes in conformation can occur.

Ellipsometry

In addition to the infrared studies, Dr. Leslie E. Smith, Carl A. Fenstermaker and Stromberg have used ellipsometry to investigate the conformational changes that occur in proteins adsorbed on various synthetic surfaces. Ellipsometry is an optical technique that determines the refractive index and thickness of very thin films by measuring the change in the state of polarized light reflected from the adsorbing surface. The method was adapted to polymer adsorption studies by Stromberg and coworkers in the mid-1960's.

These studies revealed that the amount of prothrombin, fibrinogen and serum albumin adsorbed from physiological concentrations remained approximately constant for a number of materials of varying surface energy. However, the thickness of the protein film (a measure of the extension of the protein from the surface) changed as the surface energy of the material changed. In particular, the higher the surface energy of the material, the thinner the film.

The investigators hope that the results of current and future investigations will provide a correlation between material properties of implants and blood clotting on synthetic implants, which, in turn, may help provide a rational approach to the selection of implant materials. □

HIGHLIGHTS

Design Criteria Delivered

Design criteria to attain energy conservation in new buildings have been delivered to the National Conference of States on Building Codes and Standards (NCSBCS) by NBS. The criteria were prepared by NBS in response to a request from NCSBCS.

The executive committee of NCSBCS immediately transmitted them to the American Society of Heating, Refrigerating and Air Conditioning Engineers, which will sponsor the criteria through the consensus procedure of the Nation's voluntary standards-generating system.

Productivity Conference

The third conference on "Productivity Improvement in the Service Sector of the 'National Economy'" will be held on the campus of Franklin Pierce College, Rindge, New Hampshire, July 28 to August 4, 1974.

Sponsors of the conference are the National Commission on Productivity, the Engineering Foundation and NBS. At the conference, representatives of government, labor, industry, education and the public will assess their role in the use of information transaction technology to increase the productivity of service industries and to identify significant issues for consideration at the policy level.

Attendance is by invitation or application only. Information and applications are available from the Engineering Foundation, 345 East 47th Street, New York, N.Y. 10017, telephone 212/752-6800, ext. 294, or Edwin J. Istvan, B268 Technology Building, NBS, Washington, D.C. 20234.

Storm, Quake Damage

The extensive loss of life and property caused in developing countries by earthquakes and windstorms may be considerably reduced by the adoption and implementation of improved design, siting and construction procedures discussed a new report from NBS. The report provides technical information on characteristics of materials and building systems, discusses the structural performance of buildings subjected to the action of earthquakes and wind forces and describes ways in which structures can be made more resistant to such action.

The report, designated BSS-48, is available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, by SD Catalog No. C13.29/2:48 for \$4.85.

Mobile Home Fires

With a \$50,000 grant from the Mobile Home Manufacturers Association as partial support, NBS is starting a project to investigate potential fire problem areas in mobile homes. These homes have design features not found in other dwellings. Initial investigations will include a study of the flammability of interior wall lining materials, penetration of wall and ceiling panels by fire and the role of heating units and appliances in fire.

School for Squids

NBS is sponsoring a course in the theory and operation of superconducting quantum interference devices (SQUIDS). It will be held at the NBS Boulder laboratories from July 15 through July 26, 1974.

The 2-week course of lectures and

practical laboratory experience is designed to give participants a thorough understanding of SQUIDS and their adaptation to various sensing and measuring systems.

For information, contact Dr. R. A. Kamper, Cryogenics Division, NBS, Boulder, Colo. 80302. Telephone: 303/499-1000, ext. 3535.

Measuring Cap Noise

Acoustical testing of potentially hazardous noise-producing toys have been conducted at NBS for Consumer Product Safety Commission. A new NBS report, Technical Note 793, discusses in detail the testing of commercial cap guns and caps. The work culminated in the development of a standard firing apparatus for testing paper caps. Included in the report are engineering drawings of the apparatus as well as a recommended procedure for its use.

NBS Technical Note 793 is available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, as SD Catalog No. C13.46:793 for 50 cents.

Raman Scattering

The first and second order Raman spectra of GaP have been measured at hydrostatic pressures up to 100 kbar using the gasketed diamond anvil pressure cell developed at NBS (100 kbar = 10^8 N/m²). This is the first time that Raman scattering studies have been carried out at such high pressures. The measurements reveal the high-pressure dependence of the phonon dispersion relations throughout the entire Brillouin zone. This information should help to resolve the conflicting viewpoints of various lattice dynamical theories. □



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